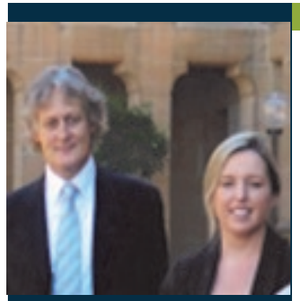

Our Aim

To develop new treatments that reduce blindness from macular disease, through multi -disciplinary, patient oriented, world class research

CONTACT US

Laboratory team

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What's in the "pipeline" for the treatment of Macular Degeneration?

"Eylea" (aflibercept) was approved for use and funded by the Australian Government last December. It is claimed by the company that sells it to be a stronger Vascular Endothelial Growth Factor (VEGF) inhibitor that lasts longer than the others (Lucentis, Avastin), but the clinical evidence for this currently is inconclusive. If it were then this would be a real advantage, but on the other hand we have only been using it in clinical practice for 1 year, whereas we have been using the other drugs for nearly seven years so their safety is perhaps better established. Many doctors are trying Eylea if patients do not respond well to Lucentis, perhaps patients may switch from Eylea to Lucentis in future as well. The good news is that we have another option .

"Fovista"-a recent "Phase 2" study suggested that patients receiving this drug as a second injection in combination with Lucentis got better improvements in vision than those treated with Lucentis alone. A phase 3 study will begin this year. If that is successful we can expect the drug to become available around 2017.

Radiation treatment

Two significant studies have recently reported. The INTREPID study found that that eyes receiving radiotherapy with the "Oraya" device had similar vision outcomes but needed fewer injections of Lucentis. The CABERNET study, which used radiation in a different way, failed to show a similar benefit. It looks like more research may be required to identify the best way to use these treatments.

A lot of work continues to be done on **Stem Cells**. Two patients who were totally blind that were treated in Los Angeles thought they could see a bit better, but they may have been imagining it. Having reported encouraging results in blind mice (there were more than 3) by transplanting photoreceptors, investigators at the Institute of Ophthalmology are planning a small clinical trial next year. It is likely that we will get stem cell treatments eventually for AMD, but nobody can say when.

To make a donation to support the Macular research team at the Save Sight Institute and the Sydney Eye Hospital, you may send a cheque to Professor Gillies made out to the "Macular Research Group" at the address on page 3. No amount is too small or too large, or you may consider remembering us when you make your will. Some people may not be in a position to give anything, and that's OK as well. We realise that many people with macular disease are pensioners. Funds from this mail-out will be used to support these and other exploratory projects of the Macular Research Group.

MacularNEWS

6th Edition

AUTUMN 2013

http://sydney.edu.au/medicine/mac

The Macular Research Group Laboratory Research Group

In this 6th edition of MacularNEWS we present examples of two of our "exploratory" laboratory research projects. We conduct these to provide background data that serve as "proof of concept" for major applications to bodies such as the National Health and Medical Research Council, which is where we get most of our funding. NHMRC is extremely competitive though, with less than 20% of applications funded in the last round. In fact, we direct much of the funding we receive from private donors to these exploratory research projects. Granting bodies rarely give money unless preliminary data can be shown, so supporting this exploratory research is always a challenge.

Research into the earliest stages of macular degeneration

Age-related macular degeneration (AMD) causes more Australian adults to go blind every year than any other disease. While regular injections into the eye of "Vascular Endothelial Growth Factor Inhibitors" (eg Lucentis, Eylea, Avastin) can be very effective for the "wet" form of AMD, where there is bleeding, there are still no treatments for patients with the "dry", or "atrophic" form of AMD, where holes appear in the macula without bleeding. We also do not fully understand why AMD develops in some people and not others.

We are working to understand the earliest age-related changes in the tissues that AMD affects: the photoreceptors, which are the light sensing cells of the eye, the choroid, which is the blood supply for the photoreceptors, and the layer of cells that separates them which is called the Retinal Pigment Epithelium. We are beginning to understand that healthy eyes depend on tightly regulated networks of inflammatory and immune cells. Eye tissues are damaged and vision is threatened when these networks don't work properly.

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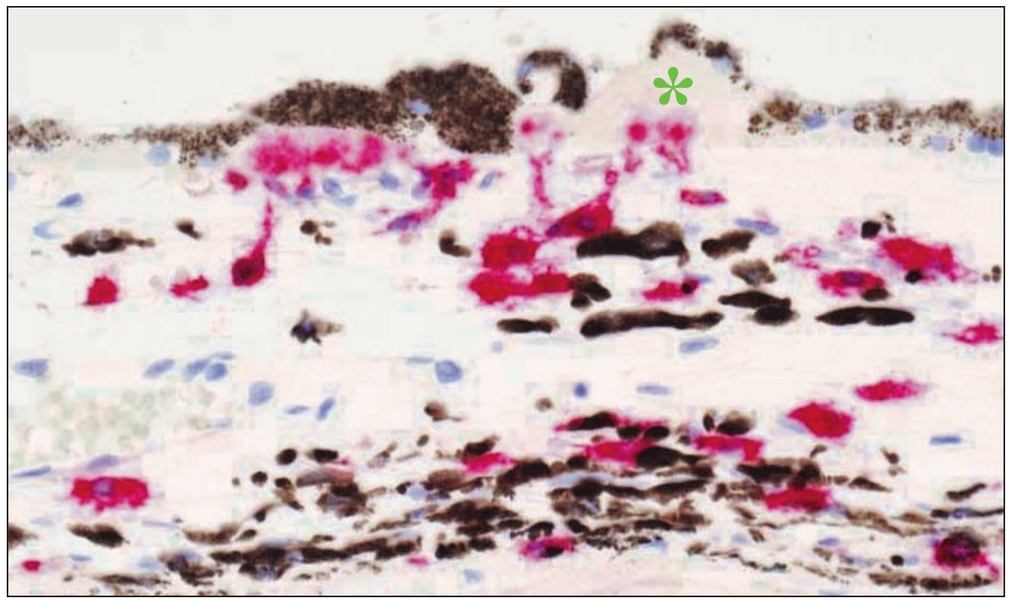
We hope to identify the disease-causing changes in these inflammatory and immune networks that set off the degenerative changes in AMD. Our long-term goal is to prevent the development of the disease in people at risk, such as the children of patients with advanced AMD.

The photograph below shows a cross section of an eye with age-related changes. The brown pigmented cells at the top are the retinal pigment epithelium. The green asterisk marks a druse (plural "drusen"), a collection of characteristic debris found beneath the retinal pigment epithelium in ageing eyes. The retinal pigment epithelium is usually a flat and smooth layer of cells but here the drusen are causing them to become irregular. Immune cells that live in the choroid, which are stained red here, extend their processes into the drusen: we think they are trying to clear the abnormal debris. Photoreceptors, which cannot be seen here, depend on healthy retinal epithelial cells for their survival. Many people aged 60 or older have drusen like these that are not yet affecting vision. We are hoping to understand how we can help the normal immune cells in the eye clear up drusen without damaging the surrounding healthy tissues and before vision starts to fail.



Dr Svetlana Cherepanoff, a pathologist, has recently joined the group to work on this project. Her start-up was made possible through a donation from Lex Elliott, a former Chief Matron of the Mater Hospital in Brisbane who had dry AMD when she died.

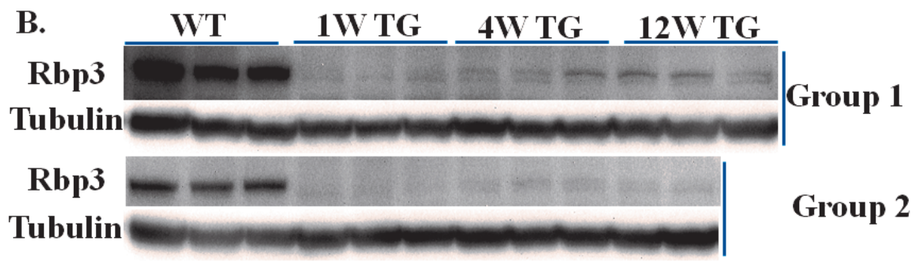
Where are we located?

You will find us at the Save Sight Institute,

South Block Sydney Hospital,
8 Macquarie Street, Sydney NSW 2000

Unexpected dysfunction of an old protein in retinal disease

Several decades ago, scientists discovered the gene for "Retinol binding protein 3" (RBP3) in retinas. RBP3 was found to be important to the "visual cycle", the process that produces the molecules that turn light into vision. Two observations that we made by chance working on other projects over the last 2 years suggest that dysfunction of RBP3 may be involved in common, vision threatening retinal diseases such as Diabetic Retinopathy, Age related Macular degeneration (AMD) and Macular Telangiectasia (Mactel). First, we found high levels of antibodies to RBP3, which might inhibit its function, in the blood of people with MacTel or AMD. Then we found, in a mouse model of retinal disease that we have described in a previous edition of *MacularNEWS (4th Edition)*, that RBP3 suddenly disappears when we switch on the retinal degeneration. Now we are working on ways to boost RBP3 function in animal models of macular disease, either with traditional drug therapy or with gene therapy in which we can make retinal cells produce more of the RBP3 protein, that they appear to be lacking.



This figure shows levels of RBP3 protein from 3 retinas per group in normal mice ("WT" = wild-type) and mice after 1 week, 4 weeks and 12 weeks after switching on the retinal degeneration ("TG" = transgenic). How we switch on the degeneration in transgenic mice is a bit complicated but it is a standard scientific technique. RBP3 levels drop dramatically as soon as the degeneration starts. Compare this with the levels of the "housekeeping" protein, tubulin, which is not expected to change in diseased retinas.

This research is being conducted by Dr Ling Zhu, a postdoctoral scientist in our lab who has advanced expertise in molecular biology. Ling moved here three years ago from a lab in the US.